PATENT COOPERATION TREATY

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INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY
(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference CWY/8116656	**FOR FURTHER ACTION** See Form PCT/IPEA/416	
International application No. PCT/SG2004/000103	International filing date *(day/month/year)* 21.04.2004	Priority date *(day/month/year)* 21.04.2003
International Patent Classification (IPC) or national classification and IPC C12Q1/70, C12Q1/68		
Applicant GENOME INSTITUTE OF SINGAPORE et al.		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 11 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. ☐ *sent to the applicant and to the International Bureau)* a total of sheets, as follows:
      ☐ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:

☒	Box No. I	Basis of the opinion
☐	Box No. II	Priority
☒	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☒	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☐	Box No. VI	Certain documents cited
☐	Box No. VII	Certain defects in the international application
☐	Box No. VIII	Certain observations on the international application

Date of submission of the demand	Date of completion of this report
18.11.2004	02.05.2005
Name and mailing address of the international preliminary examining authority: European Patent Office - P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Pays Bas Tel. +31 70 340 - 2040 Tx: 31 651 epo nl Fax: +31 70 340 - 3016	Authorized Officer Pinta, V Telephone No. +31 70 340-4049

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/SG2004/000103

Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This report is based on translations from the original language into the following language , which is the language of a translation furnished for the purposes of:
   - ☐ international search (under Rules 12.3 and 23.1(b))
   - ☐ publication of the international application (under Rule 12.4)
   - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the **elements*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

Description, Pages

1-71 as originally filed

Claims, Numbers

1-32 as originally filed

Drawings, Sheets

1/18-18/18 as originally filed

☒ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing

3. ☐ The amendments have resulted in the cancellation of:
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

* *If item 4 applies, some or all of these sheets may be marked "superseded."*

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/SG2004/000103

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 1-32 (all partially)

because:

☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (specify):

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for the said claims Nos. 1-32 (all partially)

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form
☐ has not been furnished
☐ does not comply with the standard

the computer readable form
☐ has not been furnished
☐ does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☒ See separate sheet for further details

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/SG2004/000103

Box No. IV Lack of unity of invention

1. ☐ In response to the invitation to restrict or pay additional fees, the applicant has:
   - ☐ restricted the claims.
   - ☐ paid additional fees.
   - ☐ paid additional fees under protest.
   - ☐ neither restricted nor paid additional fees.

2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is

   ☐ complied with.

   ☒ not complied with for the following reasons:

   see separate sheet

4. Consequently, this report has been established in respect of the following parts of the international application:

   ☐ all parts.

   ☒ the parts relating to claims Nos. 1-32 (all partially) .

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-32
	No:	Claims	
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-32
Industrial applicability (IA)	Yes:	Claims	1-32
	No:	Claims	

2. Citations and explanations (Rule 70.7):

   see separate sheet

Supplemental Box relating to Sequence Listing

Continuation of Box I, item 2:

1. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this report has been established on the basis of:

   a. type of material:

   ☒ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material:

   ☒ in written format

   ☒ in computer readable form

   c. time of filing/furnishing:

   ☐ contained in the international application as filed

   ☐ filed together with the international application in computer readable form

   ☒ furnished subsequently to this Authority for the purposes of search and/or examination

   ☒ received by this Authority as an amendment on

2. ☒ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

3. Additional observations, if necessary:

Reference is made to the following documents; the documents D4-D5 were not cited in the international search report.

D1: Drosten et al., New England Journal of Medicine 348 (20) 1967-1976, published on-line on 10-04-2003.

D2: Ksiazek et al., New England Journal of Medicine 348 (20) 1953-1966, published on-line on 10-04-2003.

D3: Database EMBL, Sequence Version Archive, SARS Coronavirus Tor2, complete genome, 15-04-2003, database accession number AY274119.1.

D4: Database EMBL, Sequence Version Archive, SARS Coronavirus CUHK-W1, complete genome, 18-04-2003, database accession number AY278554.1.

D5: Database EMBL, Sequence Version Archive, SARS Coronavirus HKU-39849, complete genome, 19-04-2003, database accession number AY278491.2.

D6: ROTA P A ET AL: "Characterization of a novel coronavirus associated with severe acute respiratory syndrome" SCIENCE, AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE,, US, vol. 300, no. 5624, 30 May 2003 (2003-05-30), pages 1394-1399.

Re Item IV

Lack of unity of invention

1 The IPEA agrees with the objection put forward by the ISA as to lack of unity; the arguments presented in the annex to the Partial Search Report (Invitation to pay additional fees; form PCT/ISA/206) are fully maintained [see also PCT Preliminary Examination Guidelines 10.71-10.77]. Said arguments are hereby restated:

2 The single general concept underlying the present application may be regarded as the provision of nucleic acids for the detection of a severe acute respiratory syndrome (SARS) coronavirus.

3 D1 and D2 disclose nucleic acids for the detection of a SARS coronavirus (D1: Table 1, fig. 1B; the oligonucleotides SAR1S and SAR1As are also referred to in the present application as SEQ ID NO: 13 and SEQ ID NO: 14 (p. 69, l. 2 and l. 5); D2: p. 1956, col. 1, SARS-specific primers Cor-p-F2, Cor-p-F3, Cor-p-R1).

4 In view of this prior art, this single general concept underlying the present application is not novel.

5 The applicant submitted in his letter dated 07.03.2005 that the fact that the SEQ ID NO: 1-12 and 15-24 are all derived from the same genomic region of SARS-CoV which encodes RdRp (see also the description, p. 31, first paragraph) should be seen as a unifying concept. However, such a concept cannot be seen as inventive for the following reasons. Nucleic acids for the detection of the SARS-CoV are known from the prior art (D1, D2). The concept proposed differs from this prior art in that the nucleic acids are chosen in the region which encodes RdRp, which is highly conserved in many CoVs (description p. 2, l. 25). The technical effect of this difference may be seen in that the nucleic acids provided can be utilized to detect the virus independent of the particular SARS CoV viral type. The problem to be solved may be seen in the provision of nucleic acids that can be utilized to detect the virus independent of the particular SARS CoV viral type. The solution proposed is that the nucleic acids are chosen in the region which encodes RdRp. However, it is well known to the skilled person that, in order to avoid that a detection process be limited to a particular (sub)group of organisms, nucleic acids to be used in said detection process should target sequences conserved amongst the group of organisms to detect. Since the genomic sequences of several SARS-CoV strains were available before the date of filing of the present application (D3-D5; please note that the sequences of documents D4-D5 are referred to in D6, cited in the international search report), the skilled person looking for nucleic acids that can be utilized to detect the virus independent of the particular SARS CoV viral type would have looked for conserved regions amongst which RdRp would have been identified as an obvious possibility. Accordingly, the fact that the nucleic acids of SEQ ID NO: 1-12 and 15-24 are chosen in the RdRp region cannot be seen as a single general inventive concept.

6 The problem solved by the present application may be regarded as the provision of further nucleic acids for the detection of a SARS coronavirus. The solutions proposed consist in each of the SEQ ID NO: 1-12 and 15-24.

7 In view of the above, and since the solutions brought to the problem appear to be technically unrelated and no other technical feature could be distinguished which, in light of the prior art, could be regarded as a special technical feature in the sense of Rule 13.2

PCT, the IPEA is of the opinion that there is no single inventive concept unifying inventions 1-21 in the sense of Rule 13.1 PCT.

1.1 Invention 1: claims 1-32 (all partially)
Oligonucleotide consisting of SEQ ID NO: n, or comprising a nucleic acid having at least 90% sequence identity to SEQ ID NO: n or a complement thereof, and having a length of 100 or fewer nucleotides, method of detecting a severe acute respiratory syndrome (SARS) coronavirus in a sample comprising contacting nucleic acids from the sample with at least one primer comprising SEQ ID NO: n, method of determining a presence of a SARS coronavirus in a sample comprising contacting nucleic acids and/or amplicons thereof with at least one oligonucleotide that comprise SEQ ID NO: n or a variant having at least 90% sequence identity to SEQ ID NO: n or a complement thereof, composition, kit and system for detecting a SARS coronavirus comprising at least one oligonucleotide comprising SEQ ID NO: n or a variant having at least 90% sequence identity to SEQ ID NO: n or a complement thereof, and system comprising a computer or computer readable medium comprising a data set corresponding to SEQ ID NO: n or a variant having at least 90% sequence identity to SEQ ID NO: n or a complement thereof, wherein SEQ ID NO: n is SEQ ID NO: 1.

1.2 Inventions 2-21: claims 1-32 (all partially)
as for invention 1, wherein:
- for invention 2, SEQ ID NO: n is SEQ ID NO: 2;
- for invention 3, SEQ ID NO: n is SEQ ID NO: 3;
- for invention 4, SEQ ID NO: n is SEQ ID NO: 4;
- for invention 5, SEQ ID NO: n is SEQ ID NO: 5;
- for invention 6, SEQ ID NO: n is SEQ ID NO: 6;
- for invention 7, SEQ ID NO: n is SEQ ID NO: 7;
- for invention 8, SEQ ID NO: n is SEQ ID NO: 8;
- for invention 9, SEQ ID NO: n is SEQ ID NO: 9;
- for invention 10, SEQ ID NO: n is SEQ ID NO: 10;
- for invention 11, SEQ ID NO: n is SEQ ID NO: 11 or SEQ ID NO: 23;
- for invention 12, SEQ ID NO: n is SEQ ID NO: 12;
- for invention 13, SEQ ID NO: n is SEQ ID NO: 15;
- for invention 14, SEQ ID NO: n is SEQ ID NO: 16;
- for invention 15, SEQ ID NO: n is SEQ ID NO: 17;

- for invention 16, SEQ ID NO: n is SEQ ID NO: 18;
- for invention 17, SEQ ID NO: n is SEQ ID NO: 19;
- for invention 18, SEQ ID NO: n is SEQ ID NO: 20;
- for invention 19, SEQ ID NO: n is SEQ ID NO: 21;
- for invention 20, SEQ ID NO: n is SEQ ID NO: 22;
- for invention 21, SEQ ID NO: n is SEQ ID NO: 24.

6 Since only invention 1 was the object of an International Search Report, the present written opinion is restricted to the subject-matter of said invention 1.

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1 Novelty (Art. 33(2) PCT)

1.1 In view of the prior art cited, where no oligonucleotide of 100 nucleotides or less comprising a nucleic acid of sequence corresponding to SEQ ID NO: 1 or having at least 90% sequence identity with SEQ ID NO: 1 could be identified, the subject-matter of claims 1-32 is new.

2 Inventive step (Art. 33(3) PCT)

2.1 D1 and D2 constitute equally close prior art as to the independent claims 1, 2 or 7. The subject-matter of all three claims can be summarized as an oligonucleotide comprising a nucleic acid having at least 90% sequence identity to SEQ ID NO: 1 or a complement thereof, which oligonucleotide has 100 or fewer nucleotides.

2.1.1 D1 and D2 disclose oligonucleotides for the detection of a SARS coronavirus, which oligonucleotides have 100 or fewer nucleotides (D1: Table 1, fig. 1B; the oligonucleotides SAR1S and SAR1As are also referred to in the present application as SEQ ID NO: 13 and SEQ ID NO: 14 (p. 69, l. 2 and l. 5 of the present application); D2: p. 1956, col. 1,

SARS-specific primers Cor-p-F2, Cor-p-F3, Cor-p-R1).

2.1.2 The subject-matter of claims 1, 2, or 7, differs in that the oligonucleotide comprises a nucleic acid having at least 90% sequence identity to SEQ ID NO: 1 or a complement thereof, which oligonucleotide has 100 or fewer nucleotides.

2.1.3 The problem to be solved may therefore be regarded as the provision of alternative oligonucleotides comprising nucleic acids having at least 90% sequence identity to a sequence of the SARS coronavirus or a complement thereof, which oligonucleotide has 100 or fewer nucleotides.

2.1.4 The proposed solution is an oligonucleotide comprising a nucleic acid having at least 90% sequence identity to SEQ ID NO: 1 or a complement thereof, which oligonucleotide has 100 or fewer nucleotides.

2.1.5 This solution cannot be considered as involving an inventive step for the following reasons: several complete genome sequences of the SARS coronavirus were published before the priority date of the present application, see D3-D5. Although the applicant argues in his letter dated 07.03.2005 that neither D1, D2 nor D3 suggest sequences which are especially applicable for usage as diagnostic hybridization probes, it is submitted that (i) the design of alternative oligonucleotides for a known sequence suitable for usage as diagnostic (hybridization) probes falls within the art and abilities of the skilled person and (ii) the present application does not limit itself to hybridization probes, see e.g. claim 13 where the nucleic acids claimed are used as amplification primers. An oligonucleotide as defined under item 3.1.2. is merely one of many alternatives that the skilled person would reach when trying to solve the problem posed. Accordingly, the subject-matter of claims 1, 2 and 7 does not involve an inventive step.

2.2 Dependent claims 3-6 and 8-12 do not contain any features which, in combination with the features of any claim to which they refer, meet the requirements of the PCT in respect of inventive step.

2.3 Further, claims 13-32 do not contain any additional features which could confer an inventive step, the steps of the methods or components of the composition, kit and systems

other than the oligonucleotides being well-known in the art. Accordingly, their subject-matter is also considered to lack inventive step for the same reasons.

3 Industrial applicability (Art. 33(4) PCT)

3.1 The subject-matter of claims 1-32 is considered to be industrially applicable.